SQSTM1 gene

sequestosome 1

Normal Function

The *SQSTM1* gene provides instructions for making a protein called p62. This protein plays an important role in bone remodeling, a normal process in which old bone is broken down and new bone is created to replace it. The p62 protein helps regulate this process through its role in a chemical signaling pathway that promotes the formation of osteoclasts. Osteoclasts are specialized cells that break down bone tissue during bone remodeling.

Studies suggest that p62 may have other functions in addition to its role in bone remodeling. It may be involved in recycling worn-out cell parts and unneeded proteins (autophagy), the self-destruction of cells (apoptosis), and the body's immune responses and inflammatory reactions.

Health Conditions Related to Genetic Changes

amyotrophic lateral sclerosis

Paget disease of bone

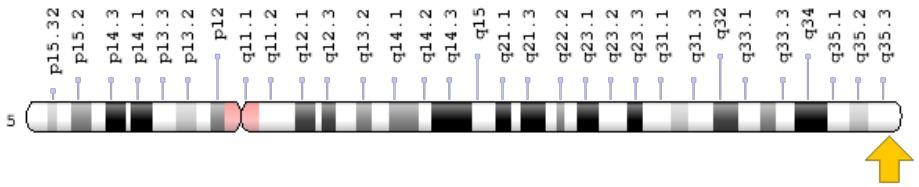
More than 20 mutations in the *SQSTM1* gene have been found to cause Paget disease of bone. Many *SQSTM1* gene mutations change single protein building blocks (amino acids) in the p62 protein. The most common mutation replaces the amino acid proline with the amino acid leucine at protein position 392 (written as Pro392Leu or P392L).

Through a mechanism that is not well understood, *SQSTM1* gene mutations appear to overactivate the chemical signaling pathway that promotes osteoclast formation. The increased signaling stimulates the production of too many osteoclasts and triggers these cells to break down bone abnormally. In people with Paget disease of bone, affected bone is broken down and replaced much faster than usual. When the new bone tissue grows, it is weaker and less organized than normal bone. These problems with bone remodeling cause certain bones to become unusually large, misshapen, and easily broken (fractured). It is unclear why the disease affects some bones but not others.

Chromosomal Location

Cytogenetic Location: 5q35.3, which is the long (q) arm of chromosome 5 at position 35.3

Molecular Location: base pairs 179,806,388 to 179,838,078 on chromosome 5 (Homo sapiens Annotation Release 108, GRCh38.p7) (NCBI)



Credit: Genome Decoration Page/NCBI

Other Names for This Gene

- A170
- EBI3-associated protein p60
- OSIL
- oxidative stress induced like
- p60
- p62
- p62B
- PDB3
- phosphotyrosine independent ligand for the Lck SH2 domain p62
- SQSTM_HUMAN
- ubiquitin-binding protein p62
- ZIP3

Additional Information & Resources

Educational Resources

- Molecular Biology of the Cell (fourth edition, 2002): Bone Is Continually Remodeled by the Cells Within It
  https://www.ncbi.nlm.nih.gov/books/NBK26889/#A4187

Scientific Articles on PubMed

- PubMed
  https://www.ncbi.nlm.nih.gov/pubmed?term=%28%28SQSTM1%5BTIAB%5D%29+OR+%28sequestosome+1%5BTIAB%5D%29+OR+%28p62%5BTIAB%5D%29%29+AND+%28%28Genes%5BMH%5D%29+OR+%28Genetic+Phenomena%5BMH%5D%29%29+AND+english%5Bla%5D+AND+human%5Bmh%5D+AND+%22last+3600+days%22%5Bdp%5D

OMIM

- SEQUESTOSOME 1
  http://omim.org/entry/601530

Research Resources

- Atlas of Genetics and Cytogenetics in Oncology and Haematology
  http://atlasgeneticsoncology.org/Genes/GC_SQSTM1.html
- ClinVar
  https://www.ncbi.nlm.nih.gov/clinvar?term=SQSTM1%5Bgene%5D
- HGNC Gene Family: Zinc fingers ZZ-type
  http://www.genenames.org/cgi-bin/genefamilies/set/91
- HGNC Gene Symbol Report
  http://www.genenames.org/cgi-bin/gene_symbol_report?q=data/hgnc_data.php&hgnc_id=11280
- NCBI Gene
  https://www.ncbi.nlm.nih.gov/gene/8878
- UniProt
  http://www.uniprot.org/uniprot/Q13501

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